

REMARKS

I. Status of Claims

Applicants have canceled claims 6-10, 15-18, 20 and 27-32. Claims 1-5, 11-14, 19, 21-26, and 33-41 are therefore pending following entry of this Amendment. Claims 19, 25, and 33-41 stand withdrawn from consideration. Claims 1-5, 11-14, 21-24 and 26 are under consideration.

Applicants have amended claims 1, 19, 21, and 24 to more clearly describe the organization of the promoter, IRES elements, and cistrons. Support for this amendment can be found throughout the specification and original claims. In particular, support can be found in the specification in the middle paragraph of page 4, in the first and second paragraphs of page 15, in the last paragraph of page 18, and in the organization of the vectors described in the Examples, as summarized in figure 6. In addition, claims 37-41 have been amended to depend only from pending claims. These amendments add no new matter.

Applicants note that claims 37-41 are process claims which depend from elected product claims. Upon finding the product claims allowable, Applicants respectfully request that the Office rejoin and fully examine method claims 37-41, as required by rejoinder practice under M.P.E.P. § 821.04.

II. Priority

In the Office Action mailed September 22, 2005, the Office states that Applicants are only entitled to the July 8, 2003, filing date of the instant application because no

reference to the priority application appears in the first line of the specification. Office Action, page 3.

Applicants respectfully note that the first line of the specification was amended on October 30, 2003, to recite the priority claim to the provisional application. Applicants direct the Office's attention to the single page Image File Wrapper entry dated October 30, 2003, and entitled "Specification." That claim for priority was made within sixteen months of the filing date of the prior application, thus no petition was required. Accordingly, Applicants request that the Office acknowledge the correct priority date of the record.

III. Rejections Based Upon "Variant", "Fragment", and "Homolog"

The Office rejects claims 1-18, 21-24, 26-30 and 32 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Office Action, page 5. According to the Office, "variants or fragments of an IRES from EV71, HCV or EMCV that would function as an IRES in the expression vectors" are not adequately described. *Id.*

In addition, the Office rejects claims 6-10, 15-18, 27-30 and 32 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. *Id.* at 6. The Office asserts that "there is not a structural and functional relationship provided by the prior art or the specification for one of skill in the art to envision all the structures that are homologs of an IRES from EV71, HCV or EMCV and possess the same function as an IRES from these viruses." *Id.* at 7.

Finally, the Office rejects claims 1, 6, 21, 24, 27 and 30 under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter of the invention. *Id.* Here the Office finds that “the phrase ‘variant or fragment thereof’ does not define the scope of the limitations.” *Id.*

Applicants traverse those grounds of rejections. However, solely to expedite prosecution, Applicants have canceled claims 6-10, 15-18, and 27-32 and amended claims 1, 21, and 24. Applicants respectfully submit that those amendments obviate the rejections under 35 U.S.C. § 112, first and second paragraphs. Accordingly, Applicants request that the Office withdraw those rejections.

IV. Rejections Under 35 U.S.C. § 102

A. Urabe

The Office contends that claims 1-5, 11 and 13 are anticipated under 35 U.S.C. § 102(b) by Urabe *et al.*, Gene, Vol. 200, pp. 157-62 (1997) (“Urabe”). Office Action, page 8. According to the Office, Urabe teaches expression of a dicistronic adeno-associated vector comprising a CMV promoter, a reported gene or a therapeutic gene, either the HCV or EMCV IRES, and a selectable marker expressed in mammalian cells. *Id.*

Applicants have amended claim 1 to recite that at least one nucleotide sequence comprises an IRES sequence from EV71. Urabe does not teach a dicistronic vector comprising an IRES sequence from EV71. Applicants therefore respectfully request the Office withdraw the rejection.

B. van Zonneveld

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,447,768 to van Zonneveld *et al.* ("van Zonneveld"). Office Action, page 8. van Zonneveld is said to teach "a dicistronic adenoviral vector that comprises a CMV promoter, NO synthase cDNA, IRES from EMCV and VEGF or FGF4 cDNA as the angiogenic factors and cells containing the adenoviral vector. *Id.*

As with Urabe, van Zonneveld does not teach a dicistronic vector comprising an IRES sequence from EV71. Claim 1 as amended recites that at least one of the nucleotide sequences that provide IRES activity comprises an EV71 IRES. Applicants therefore respectfully request the Office withdraw the rejection.

C. Whitley

Claims 1, 3-5, 11 and 13 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,764,675 to Whitley *et al.* ("Whitley"). Office Action, page 9. The Office relies upon Whitley as teaching "a dicistronic herpes simplex virus (HSV) vector that comprises an Egr-1 promoter, the p40 and p35 subunits of mIL-12 separated by an IRES from EMCV and mammalian cells containing the vector. *Id.*

Applicants have amended claim 1 to recite that at least one of the nucleotide sequences that provide IRES activity comprises an IRES sequence from EV71. Whitley does not teach a dicistronic vector comprising an IRES sequence from EV71. Applicants therefore respectfully request the Office withdraw the rejection.

D. Agarwal

The Office also rejects claims 1-5, 11 and 13 under 35 U.S.C. 102(b) as allegedly anticipated by U.S. Patent No. 6,194,212 to Agarwal *et al.* ("Agarwal"). Office Action, page 9. According to the Office, Agarwal teaches "a dicistronic retroviral vector comprising a retroviral promoter such as LTR and an IRES from EMCV separating the RevM10 gene and the marker gene Lys-2 and cells containing the retroviral vector." *Id.*

As with the other cited references, Agarwal does not teach a dicistronic vector comprising an IRES sequence from EV71. Claim 1 as amended recites that at least one of the nucleotide sequences that provide IRES activity comprises an EV71 IRES. Applicants therefore respectfully request the Office withdraw the rejection.

E. Seguela

The Office also rejects claims 1, 3-5, 11 and 14 under 35 U.S.C § 102(b) as allegedly anticipated by Seguela *et al.* (US 2003/0219858) ("Seguela"). Office Action, page 10. According to the Office, Seguela teaches "a bicistronic nucleic acid vector that comprises a CMV promoter and two nucleotide sequences encoding ASIC2A and ASIC3 polypeptides separated by an IRES from EMCV and E. coli cells containing the vector." *Id.*

Applicants have amended claim 1 to recite that at least one of the nucleotide sequences that provide IRES activity comprises an IRES sequence from EV71. Seguela does not teach a dicistronic vector comprising an IRES sequence from EV71. Applicants therefore respectfully request the Office withdraw the rejection.

E. Finkelstein

Claims 1, 2, 4, 5, 11, 12, 21, 22, 24, and 26 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Finkelstein *et al.*, J. Biotechnol. Vo. 75, pp. 33-44 (1999) ("Finkelstein"). Office Action, page 10. The Office states that "Finkelstein et al teaches a bicistronic baculovirus vector that comprises a baculovirus polyhedrin promoter (Ppol) and an EMCV IRES separating two reporter genes such as chloramphenicol transferase (CAT) and firefly luciferase (LUC) and recombinant baculoviruses." *Id.*

Applicants have amended claims 1, 21 and 24 to recite that at least one of the nucleotide sequences that provide IRES activity comprises an IRES sequence from EV71. Finkelstein does not teach a dicistronic vector comprising an IRES sequence from EV71. Applicants therefore respectfully request the Office withdraw the rejection.

V. Rejections Under 35 U.S.C. § 103(a)

A. Urabe in view of Kirkegaard

The Office rejects claims 1-5, 11 and 13 under 35 U.S.C. § 103(a) as unpatentable over the combination of Urabe and Kirkegaard et al. (US 2004/0052765) ("Kirkegaard"). Office Action, page 12. The Office reiterates its position regarding the teachings of Urabe, but acknowledges that Urabe does not teach a poxvirus. *Id.* Nevertheless, the Office points to Kirkegaard as teaching a dicistronic vaccinia virus vector comprising a poliovirus IRES, and asserts that the ordinary artisan would have been motivated to modify the teachings of Urabe to incorporate a poxvirus vector. *Id.*

Applicants traverse the Office's position, but note that the neither Urabe nor Kirkegaard teach an EV71 IRES. Claim 1 as amended recites that at least one of the

nucleotide sequences that provide IRES activity comprises an EV71 IRES. The cited references, therefore, do not teach or suggest every limitation of the claims. Applicants respectfully request the Office to withdraw the rejection.

B. Finkelstein in view of Urabe

The Office also rejects claims 1-5, 11-13, 21-24 and 26 under 35 U.S.C. § 103(a) “as being unpatenable over Urabe et al. . . . in view of Kirkegaard et al. (US 2004/0052765 A1).” Office Action, page 13. Because the body of the rejection discusses Finkelstein in view of Urabe, *id.*, Applicants have interpreted those references to be the basis of the rejection of claims 1-5, 11-13, 21-24 and 26. In this rejection, the Office asserts that the ordinary artisan would have found it obvious to modify the teachings of Finkelstein to obtain a baculovirus expression vector comprising two cistrons separated by an IRES by HCV, because Urabe teaches that either an HCV or EMCV IRES can be used in a dicistronic AAV vector. *Id.*

Applicants traverse the Office's position. Neither Finkelstein nor Urabe teach an EV71 IRES. Each of claims 1, 21 and 24 as amended recite that at least one of the nucleotide sequences that provide IRES activity comprises an EV71 IRES. The cited references, therefore, do not teach or suggest every limitation of the claims. Accordingly, Applicants respectfully request that the Office withdraw the rejection.

CONCLUSION

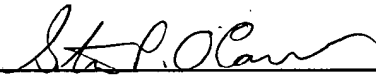
In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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